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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,545	04/09/2004	Michael E. Hepperle	MPI03-043P1RNM	1299

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MILLENNIUM PHARMACEUTICALS, INC.
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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	**PAPER NUMBER**
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,545	HEPPERLE ET AL.	
	Examiner	Art Unit	
	Rebecca L. Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9,17,19-25 and 28-34* is/are pending in the application.

4a) Of the above claim(s) *19-25 and 30-34* is/are withdrawn from consideration.

5)☒ Claim(s) *28 and 29* is/are allowed.

6)☒ Claim(s) *1, 9 and 17* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 9, 17, 19-25 and 28-34 are currently pending in the instant application. Claims 28 and 29 appear allowable, claim 1 is objected, claims 1, 9 and 17 are rejected and claims 19-25 and 30-34 are withdrawn from consideration as being for non-elected subject matter.

Response to Amendment

Applicants' amendment filed 29 October 2007 and Applicants' arguments filed 21 August 2007 have been considered and entered into the application. Applicants' amendment has overcome the claim objection of claims 1, 8, 9 and 16-18 as containing non-elected subject matter; has overcome the claim objection of claims 12 and 12; has overcome the 35 USC 112 2nd paragraph rejection of claims 11-13 and 15; and has overcome the 35 USC 112 2nd paragraph rejecti^{on} of claim 29. The 35 USC 112 2nd paragraph rejection of claims 1, 9 and 17 is maintained in regards to the "amino acid side chains". While applicant has stated that the provisional nonstatutory obviousness-type double patenting rejection of claims 1, 9 and 17 will be addressed when allowable subject matter is indicated, it is noted that as the provisional rejection is considered proper, and it is therefore maintained. The 35 USC 103(a) rejection of claims 1, 9 and 17 is maintained.

In regards to the 35 USC 112 2nd paragraph rejection of claims 1, 9 and 17 over "amino acid side chains" Applicants argue that one of ordinary skill in the art can readily determine what an amino acid side chain is and that it is well-known that the structure of amino acids consist of "an amino group, a carboxy group, a hydrogen atom, and a

distinctive R group bonded to a carbon atom and that the R group is referred to as a side chain. This argument is not persuasive as the definition of an amino acid side chain provided by applicant is a variable R which does not provide a definition of an "amino acid side chain" as it is indefinite as it fails to particularly point out and distinctly disclose the subject matter which applicant regards as the invention. The phrase "amino acid side chains" is unclear as there is no guidance on how to determine if a substituent is an "amino acid side chain as hydrogen, C1-6aliphatic, phenyl and benzyl are not considered amino acid side chains as they are defined as different values for R12. While amino acids can be natural and unnatural amino acids. It is unclear what side chains are considered amino acid side chains since hydrogen, C1-6aliphatic, phenyl and benzyl are not considered amino acid side chains. It is unclear what are "amino acid side chains" as there is no guidance on how to determine if a substituent is an "amino acid side chain". Additionally, page 16 still does not provide a definition for what these side chains are and are not. What side chains are considered "amino acid side chains" and how is one to determine what side chains are and are not amino acid side chains.

In regards to the 35 USC 103(a) rejection of claims 1, 9 and 17, Applicants argue that in order to establish a prima facie case of obviousness 1) there must be some suggestion or motivation to modify the reference; 2) there must be a reasonable expectation of success; and 3) the prior art reference must teach or suggest all of the claim limitations. These arguments are not persuasive as 1) the motivation to make the claimed compounds derives from the expectation that structurally similar compounds

would possess similar activity (ie., inhibitors of IKK, see wherein compound 35 has a listed IC50 value); 2) the reasonable expectation of success is seen in that it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963); and 3) the prior art reference teaches and suggests all of the claim limitations as Castro et al discloses the compound 35 and registry no. 590398-98-4 useful to inhibit IKK for the treatment of certain inflammatory diseases (pages 2419 and 2421 and abstract) and the only difference between the prior art and the claims at issue is that the prior art provides an unsubstituted ring A wherein ring A of the instant claims is substituted by at least one of C(R9)3, W-G or G, wherein C(R9)3 can be methyl. Therefore, the difference between the instant claims and the prior art can be a hydrogen versus a methyl on the morpholine ring which is a suggested difference as it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. While applicant argues that Castro teaches away from the use of morpholine substituents, as the compound 35 has an IC50 of greater than 20, it is noted that Castro teaches that compound 35 does have IKK activity which provides motivation to prepare additional compounds useful for the inhibition of IKK. The rejection is therefor maintained.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied

with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/461,468 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Specifically, claims 1, 9, 17, 28 and 29 are not entitled to the benefit of the prior application as subject matter found in the instant claims does not find support in Application No. 60/461,468. For example, wherein Ring A is a morpholinyl that is substituted by (i), (ii) and (iii) does not find support in the prior-filed application as the prior-filed application only provides support for morpholinyl attached at the 3-position with specific substituents. Additionally, wherein R1 is halo and R3 is cyano also does not find support in the prior-filed application as the prior-filed application does not allow or provide a definition for R1 and R3 as halo or cyano, respectively.

Accordingly, claims 1, 9, 17, 28 and 29 are not entitled to the benefit of the prior application.

New Claim Objections

Claim 1 is objected to because of the following informalities: Specifically, claim 1 has Ring A defined as a morpholinyl ring, however, group (iii) which is substituted on the morpholinyl ring states that the substituent can be "0-2 oxo groups on a ring sulfur". It is suggested that "or 0-2 oxo groups on a ring sulfur" be deleted from the definition of ring A substituents since morpholine does not have a ring sulfur. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 9 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the phrase "amino acid side chain" renders the claims indefinite as it is unclear what substituents are considered "amino acid side chains". Pages 15 of the specification states that R12 can be hydrogen, C1-6aliphatic, substituted or unsubstituted phenyl, substituted or unsubstituted benzyl or an amino acid side chain. Therefore, hydrogen, C1-6aliphatic, phenyl and benzyl are not considered amino acid side chains as they are defined as different values for R12. Amino acids can be natural and unnatural amino acids. It is unclear what side chains are considered amino acid side chains since hydrogen, C1-6aliphatic, phenyl and benzyl are not considered amino acid side chains. It is unclear what are "amino acid side chains" as there is no guidance on how to determine if a

substituent is an "amino acid side chain". Additionally, while page 16 states that amino acid side chains are particularly side chains of a natural amino acid, this still does not provide a definition for what these side chains are and are not. What side chains are considered "amino acid side chains" and how is one to determine what side chains are and are not amino acid side chains.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9 and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3, 10, 15, 16, 19, 28 and 29 of copending Application No. 11/101998. Although the conflicting claims are not identical, they are not patentably distinct from each other because conflicting claims 3, 10, 15, 16, 19, 28 and 29 provide compounds and pharmaceutical compositions which overlap with applicants instantly claimed elected invention. Conflicting claim 3 provide products which overlap with applicants' instantly claimed elected invention. Conflicting claims 10, 15 and 16 provide preferences towards applicants' instantly claimed elected invention such as wherein the compound is (S) (claim 10); wherein G is N-piperidinyl, N-piperazinyl, N-morpholinyl or N-pyrrolidinyl (conflicting claim 15); and wherein Rb is methyl (conflicting claim 16). Conflicting claim 19 provides pharmaceutical compositions. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castro et al. (C1 reference on 1449 and U reference on 892).

Determining the scope and contents of the prior art

Castro et al discloses the compound 35 and registry no. 590398-98-4 useful to inhibit IKK for the treatment of certain inflammatory diseases (pages 2419 and 2421 and abstract).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art provides an unsubstituted ring A wherein ring A of the instant claims is substituted by at least one of C(R9)3, W-G or G, wherein C(R9)3 can be methyl. Therefore, the difference between the instant claims and the prior art can be a hydrogen versus a methyl on the morpholine ring.

Resolving the level or ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare compounds of applicants instant elected invention when faced with the prior art of Castro et al., which discloses compound 35 and registry no.590398-98-4 which are useful as inhibitors of IKK for the treatment of certain inflammatory diseases. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (ie., inhibitors of IKK).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday from 6:00am until 2:30pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Anderson/
Primary Examiner, AU 1626

7 January 2008

Rebecca Anderson
Primary Examiner
Art Unit 1626, Group 1620
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